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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,725	10/01/2003	Michael G. Rosenblum	CLFR:029USD1	2944

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EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/676,725	ROSENBLUM, MICHAEL G.	
	Examiner	Art Unit	
	Laura B. Goddard, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,7,10,13,14,16,21 and 23-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,13,14,16,23,24 and 26-29* is/are rejected.

7)☒ Claim(s) *10,21 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed December 13, 2005 in response to the Office Action of September 14, 2005, is acknowledged and has been entered. Previously pending claims 5, 10, 21, and 25 have been amended. Claims 5, 7, 10, 13, 14, 16, 21, 23-29 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Objections

3. Claims 10, 21 and 25 appear to be free of the art but are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Maintained Rejection

Claim Rejections - 35 USC § 112

4. Claims 5, 7, 13, 14, 16, 23, 24, and 26-29 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

5. Applicant submitted deposit information for monoclonal antibody ZME-018 to describe a ZME-018 antigen that is recognized by monoclonal antibody ZME-018 (as recited in claims 10, 21, and 25), however, Applicant fails to address the written description requirement for claims 5, 7, 13, 14, 16, 23, 24, and 26-29.

New Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 5, 7, 13, 14, and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 4,971,792, Steplewski et al, filed 3/27/1987.

The claims are drawn to a method of treating cancer in a human patient comprising (a) determining that the cells of the patient's cancer express a selected cell surface associated antigen that can be recognized and bound by a protein with an antigen recognition site directed to the antigen; and (b) administering to a patient determined to have cancer whose cells express such an antigen a cytocidally effective dose of a composition comprising said protein conjugated or fused to a biological

response modifier (claim 5, 24), wherein said cancer is breast cancer (claim 7), wherein the biological response modifier is a cytokine and is TNF (claims 13 and 14), and

US Patent 4,971,792 teaches a successful method of treating breast cancer in patients comprising identifying antigenic expression of a biopsy sample from the patient using a monoclonal antibody that specifically binds the antigen expressed on the surface of the tumor cells, and administering the monoclonal antibody that recognizes the tumor antigen to the patient (col. 11, lines 1-26; col. 2, lines 11-15). US Patent 4,971,792 teaches monoclonal antibodies conjugated to biological response modifiers which include cytokines such as TNF (col. 7, lines 44-55; see claims 1, 8 and 9).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 4,971,792, Steplewski et al, filed 3/27/1987, in further view of US Blick et al (Cancer Research, 1987, 47:2986-2989, previously recited).

The claims are drawn to the method of claim 5 wherein the TNF is TNF-α (claim 16).

US Patent 4,971,792 teach a method of treating cancer in a human patient and a monoclonal antibody conjugated to TNF as set forth above. US Patent 4,971,792 does not teach a method wherein the TNF is TNF-α.

Blick et al teach a method of treating cancer in a human patient with TNF-alpha with evidence of anti-tumor effects for some patients (p. 2988, col. 1; p. 2989, col. 1). It is well known in the art and the reference teaches that cytokines such as TNF-α are known to have cytostatic and cytotoxic effects against a wide range of human tumor cells.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the cytokine TNF-α as a biological response modifier because TNF-alpha is a well known biological response modifier that has anti-tumor activity and is a natural defense against tumors produced by activated macrophages and because US Patent 4,971,792 teaches the conjugation of a monoclonal antibody to TNF for treatment of cancer. One would have been motivated to use TNF-alpha as a biological response modifier because of its known anti-tumor effects and for the advantages of conjugating TNF-alpha to an antibody to specifically target the anti-tumor effects.

8. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 4,971,792, Steplewski et al, filed 3/27/1987, in further view of US Patent 5,135,736, Anderson et al, filed 8/15/1988.

The claim is drawn to the method of claim 5 wherein the protein with an antigen recognition site is fused to the biological response modifier (claim 23).

US Patent 4,971,792 teaches a method of treating cancer in a human patient and a monoclonal antibody conjugated to biological response modifier as set forth above. US Patent 4,971,792 does not teach a method wherein the biological response modifier is fused to the protein, or antibody.

US Patent 5,135,736 teaches the manufacture of fusion proteins comprising an antibody and a cytotoxic agent wherein the fusion protein is produced through recombinant DNA technology (col. 2, lines 16-30; col. 12, lines 55-61; Example IV). US Patent 5,135,736 teaches method for enhancing *in vivo* cytotoxicity of a targeting protein conjugate comprising administering the conjugated protein or antibody to a tumor-bearing patient and a method for enhanced *in vivo* imaging of a tumor comprising administering the same conjugated protein or antibody (col. 1, lines 55-64). US Patent 5,135,736 teaches that the formation of a covalently-linked complex, such as an antibody-cytotoxic agent fusion protein, allows increased retention of the targeted protein or antibody conjugate at the plasma membrane of a target cell (col. 14, lines 26-31).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a fusion protein as taught by US Patent 5,135,736 in the method of treating cancer taught by US Patent 4,971,792 because US Patent 5,135,736 teaches the recombinant production of an antibody fused to a cytotoxic agent. One would have been motivated to use a fusion protein comprising an antibody

used to a cytotoxic agent, such as a biological response modifier, in the method taught by US Patent 4,971,792 because US Patent 5,135,736 teaches that an antibody fused to a cytotoxic agent increases retention of the targeted protein or antibody conjugate at the plasma membrane of a target cell, hence enhancing *in vivo* cytotoxicity of the targeting fusion protein to treat the targeted cancer.

9. All other rejections recited in the Office Action mailed September 14, 2005 are hereby withdrawn.

10. Claims 10, 21 and 25 are objected to. Claims 5, 13, 14, 16, 23, 24, 26-29 are rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura B Goddard, Ph.D.
Examiner
Art Unit 1642

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER